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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/509,239	03/23/2000	CLAUDINE BRUCK	B45110	3102

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EXAMINER	
WINKLER, ULRIKE	
ART UNIT	**PAPER NUMBER**
1648	23

DATE MAILED: 06/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/509,239	BRUCK ET AL.	
	Examiner	Art Unit	
	Ulrike Winkler	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 March 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-36 and 39-78* is/are pending in the application.

4a) Of the above claim(s) *55-77* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-36, 39-54, 78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The Amendment filed March 13, 2003 (Paper No. 22) in response to the Office Action of September 10, 2002 is acknowledged and has been entered. Claims 37 and 38 have been cancelled. Claims 32-36 and 39-54 are pending and are currently being examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Claim Rejections - 35 USC § 112

The rejection of claims 37 and 38 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention **is withdrawn** in view of applicant cancellation of the claims.

The rejection of claims 37 and 38 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention **is withdrawn** in view of applicant cancellation of the claims.

The rejection of claims 32-36, 39-54 and newly added claim 78 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for Nef-Tat and fusion partner-Nef-Tat as set out in SEQ ID Nos: 12, 13, 16, 17, 20, 21, 23, 24 does not reasonably provide enablement for "mutants thereof" **is maintained** for reason of record.

Applicant's arguments have been fully considered but fail to persuade. Applicant's point to example 6 in the specification as providing the means for determining whether a "mutant thereof" is immunogenic. In order for a composition to be enabled it requires that the composition be ascertainable based on structure and function. In this instance there are no limitation placed on the structure of "mutant thereof" and the specification (example 6) merely provides that a protein must be immunogenic when injected into an animal. The specification defines a "mutant" (page 3, lines 6-9) as a molecule, which has undergone deletion, addition or substitution of one or more amino acids (this could include all amino acids) using well-known techniques. However, the specification provides no correlation between the "mutant structure" and a specific measurable relationship to the original structure. Being immunogenic is not specific enough function to ascertain a structure function relationship for the mutatns. Because of the unlimited number of mutation that are encompassed by the claims the instant invention is not enabled for the full scope as claimed comprising "mutants thereof" other than those specially disclosed in the specification.

The rejection is of claims 32-53 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention **is withdrawn** in view of applicants amendments to the claims.

Claim Rejections - 35 USC § 103

The rejection of claims 32-36, 39-54 and newly added claim 78 under 35 U.S.C. 103(a) as being unpatentable over Schluesener (Journal of Neuroscience 1996, found on 892 of paper

No. 4) and Hinkula et al. (Journal of Virology 1997), further in view of Gaynor et al. (U.S, Pat. No. 5,597,895), further in view of Berman et al. (U.S. Pat No. 5,864,027) or further in view of Forsgren (U.S. Pat. No. 5,888,517) **is maintained** for reasons of record.

Applicant's arguments have been fully considered but fail to persuade. Applicant's arguments are that the reference teaches away from the instantly claimed invention. Specifically, Schluessener et al. utilize the Tat epitopes for a different purpose such as cellular uptake and tolerance. However, upon close inspection of the actual data in the reference (see Table IA) it is apparent that not all of the combinations of Tat - peptide result in the production of tolerance when inoculated into the animals. Therefore, some produce an immunogenic response. The instant invention is drawn to a composition comprising an HIV Tat and Nef protein or "mutant thereof" linked to each other. Any peptide greater than 6 contiguous amino acids will be immunogenic when injected into an animal. The specification defines a "mutant" (page 3, lines 6-9) as a molecule, which has undergone deletion, addition or substitution of one or more amino acids using well-known techniques. The fusion proteins taught by Schluessener et al. that do not provide tolerance (for example those associated with EAU) anticipate the instant "mutants thereof" because the NEF protein contemplated by the instant invention may have experienced an undisclosed number of mutations so that it is now has the sequence of the EAU peptide. Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. *In re Susi*, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). "A known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." *In re Gurley*, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994).

Applicant further argues that neither of the primary references teache a combination of two full length proteins in a fusion state. Applicant argues that the Hinkula et al. plasmid s are not constructed in such a way as to result in the secretion of the product. There is nothing in the claims that would indicate secretion is required. It is noted that the features upon which applicant relies (i.e., secreted peptide or full-length peptide) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Furthermore, the plasmid constructs do induce antibody production against the encoded proteins (Hinkula et al., page 5529, see Table 1).

In response to applicant's argument that there is no suggestion to combine the references, because the references teach different approaches, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, each of the references teach a composition and each compositions is used for the purpose of immunization to elicit an immune response in a subject.

It remains the Offices position that the instant invention would have been obvious to one of ordinary skill in the art at the time the invention was made to formulate a polyvalent immunogen using multivalent linked/fused HIV antigens (as taught by Schluesener) as well as multiple HIV antigens (as taught by Hinkula et al.) to stimulate immune responses to HIV. The

ordinary artisan would have been motivated to provide many different peptides which can be efficiently taken up by cells in order to maximize the immune response against the pathogen. One of ordinary skill in the art at the time the invention was made would have been motivated to fuse the HIV Tat and Nef that is to be used as an immunogen following the teachings of Hinkula et al. which indicate that a successful vaccine/immunogen will require many proteins. Hinkula et al. teach a composition comprising the full length Nef, Rev, Tat, gp160 and gag in a single formulation for the injection into an animal. It would also been obvious to the ordinary artisan that when constructing the fusion protein containing many epitopes to additionally add an epitope tag (such as histidine or GST) for purposes of purification which would simplify the production of the immunogen, the motivation being the simplified procedure (see also Gaynor et al. Tat fusion with influenza tag). The references of Gaynor et al., Berman et al. or Forsgren teach the additional limitations in view of the primary references Schluesener and Hinkula et al. It is *prima facie* obvious to combine two compositions each of which is taught by prior art to be useful for the same purpose in order to form a third composition that is to be used for the very same purpose; the idea of combining them flows logically from their having been individually taught in prior art. *In re Kerkhoven*, 205 USPQ 1069, CCPA 1980. See MPEP 2144.06. Optimizing the formulation of the composition (specifically claims 43- 49), including the addition of adjuvants or protein modification (carboxymethylation) or denaturation agents fall within the skill of an ordinary artisan. If the addition of the modulating compounds produces an unexpected result, applicant needs to point out what the unexpected results are.

Therefore, the instant invention of claims 32- 54 are obvious over Schluesener and Hinkula et al. further in view of Gaynor or Berman et al. or Forsgren.

Conclusion

Claims 32-36, 39-54 and 78 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 703-308-8294. The examiner can normally be reached M-F, 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 703-308-4027.

The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for informal communications use 703-308-4426.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Ulrike Winkler, Ph.D.

James C. Housel 6/1/03

JAMES HOUSEL
SUPERVISORY PATENT EXAMINER
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